

Application No.: 09/993,844  
Amdt. Dated: October 1, 2004  
Reply to Office Action Dated: June 23, 2004



Attorney Docket No. NRK.10026  
Page 8 of 10

**Amendments to the Drawings:**

Please replace Figures 1, 2, 3, 4, 7, 8, 9, 10, and 11 with the following replacement figures that are attached hereto: Figures 1A, 1B, and 1C; 2A, 2B, 2C, and 2D; 3A and 3B; 4A, 4B, and 4C; 7A and 7B; 8A, 8B, and 8C; 9A, 9B, and 9C; 10A, 10B, 10C, 10D, and 10E; and 11A, 11B, 11C, 11D, 11E, and 11F.

No new matter has been added to the Figures.

# FIGURE 1A

## Human G Protein Coupled Receptor Family

(Receptors known as of January, 1999)

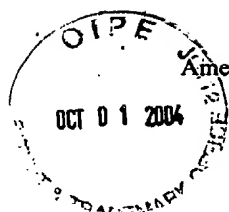
CLASS	LIGAND	NUMBER	TISSUE	PHYSIOLOGY	THERAPEUTICS
•Class I Rhodopsin like					
	•Amine				
	•Acetylcholine (muscarinic & nicotinic)	5	Brain, Nerves, Heart	Neurotransmitter	Acuity, Alzheimer's
	•Adrenoceptors				
	•Alpha Adrenoceptors	6	Brain, Kidney, Lung	Gluconeogenesis	Diabetes, Cardiovascular
	•Beta Adrenoceptors	3	Kidney, Heart	Muscle Contraction	Cardiovascular, Respiratory
	•Dopamine	5	Brain, Kidney, GI	Neurotransmitter	Cardiovascular, Parkinson's
	•Histamine	2	Vascular, Heart, Brain	Vascular Permeability	Anti-inflammatory, Ulcers
	•Serotonin (5-HT)	16	Most Tissues	Neurotransmitter	Depression, Insomnia, Analgesic
	•Peptide				
	•Angiotensin	2	Vascular, Liver, Kidney	Vasoconstriction	Cardiovascular, Endocrine
	•Bradykinin	1	Liver, Blood	Vasodilation,	Anti-inflammatory, Asthma
	•C5a anaphylatoxin	1	Blood	Immune System	Anti-inflammatory
	•Fmet-leu-phe	3	Blood	Chemoattractant	Anti-inflammatory
	•Interleukin-8	1	Blood	Chemoattractant	Anti-inflammatory
	•Chemokine	6	Blood	Chemoattractant	Anti-inflammatory
	•Orexin	2	Brain	Fat Metabolism	Obesity
	•Nociceptin	1	Brain	Bronchodilator, Pain	Airway Diseases, Anesthetic
	•CCK (Gastrin)	2	Gastrointestinal	Motility, Fat Absorption	Gastrointestinal, Obesity, Parkinson's
	•Endothelin	2	Heart, Bronchus, Brain	Muscle Contraction	Cardiovascular, Respiratory
	•Melanocortin	5	Kidney, Brain	Metabolic Regulation	Anti-inflammatory, Analgesics
	•Neuropeptide Y	5	Nerves, Intestine, Blood	Neurotransmitter	Behavior, Memory, Cardiovascular
	•Neurotensin	1	Brain,	CNS	Cardiovascular, Analgesic
	•Opioid	3	Brain,	CNS	Depression, Analgesic
	•Somatostatin	5	Brain, Gastrointestinal	Neurotransmitter	Oncology, Alzheimer's
	•Tachykinin (Substance P, NKA <sub>1</sub> )	3	Brain Nerves	Neurohormone	Depression, Analgesic

Application No. 09/993,844

Response to Office Action dated June 23, 2004

Amendment under 37 C.F.R. § 1.116 filed October 1, 2004

## REPLACEMENT SHEET



REPLACEMENT SHEET

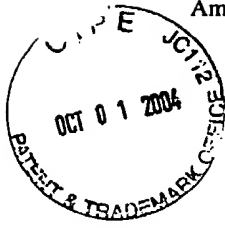
FIGURE 1B

•Thrombin	3	Platelets, Blood Vessels	Coagulation	Anti-coagulant, Anti-inflammatory
•Vasopressin-like	4	Arteries, Heart, Bladder	Water Balance	Anti-diuretic, Diabetic Complications
•Galanin	1	Brain, Pancreas	Neurotransmitter	Analgesics, Alzheimer's
•Hormone protein				
•Follicle stimulating hormone	1	Ovary, Testis	Endocrine	Infertility
•Lutropin-choriogonadotropic	1	Ovary, Testis	Endocrine	Infertility
•Thyrotropin	1	Thyroid	Endocrine	Thyroidism, Metabolism
•(Rhod)opsin				
•Opsin	5	Eye	Photoreception	Ophthalmic Diseases
•Olfactory	4(-1000)	Nose	Smell	Olfactory Diseases
•Prostanoid				
•Prostaglandin	5	Arterial, Gastrointestinal	Vasodilation, Pain	Cardiovascular, Analgesic
•Lysophosphatidic Acid	2	Vessels, Heart, Lung	Inflammation	Cancer, Anti-Inflammatory
•Sphingosine-1-phosphate	2	Most Cells	Cell proliferation	Cancer
•Leukotriene	1	White Blood Cells, Bronchus	Inflammation	Asthma, Rheumatoid Arthritis
•Prostacyclin	1	Arterial, Gastrointestinal	Platelet Regulation	Cardiovascular
•Thromboxane	1	Arterial, Bronchus	Vasoconstriction	Cardiovascular, Respiratory
•Nucleotide-like				
•Adenosine	4	Vascular, Bronchus	Multiple Effects	Cardiovascular, Respiratory
•Purinoreceptors	4	Vascular, Platelets	Relaxes Muscle	Cardiovascular, Respiratory
•Cannabis	2	Brain	Sensory Perception	Analgesics, Memory
•Platelet activating factor	1	Most Peripheral Tissues	Inflammation	Anti-inflammatory, Anti-asthmatic
•Gonadotropin-releasing hormone like				
•Gonadotropin-releasing hormone	1	Reproductive Organs, Pituitary	Reproduction	Prostate Cancer, Endometriosis
•Thyrotropin-releasing hormone	1	Pituitary, Brain	Thyroid Regulation	Metabolic Regulation
•Growth hormone- inhibiting factor	1	Gastrointestinal	Neuroendocrine	Oncology, Alzheimer's
•Melatonin	1	Brain, Eye, Pituitary	Neuroendocrine	Regulation of Circadian Cycle
•Secretin	1	Gastrointestinal, Heart	Digestion	Obesity, Gastrointestinal
•Calcitonin	1	Bone, Brain	Calcium Resorption	Osteoporosis
•Corticotropin releasing factor/lurocortin	1	Adrenal, Vascular, Brain	Neuroendocrine	Stress, Mood, Obesity
•Gastric inhibitory peptide (GIP)	1	Adrenals, Fat Cells	Sugar/Fat Metabolism	Diabetes, Obesity
•Glucagon	1	Liver, Fat Cells, Heart	Gluconeogenesis	Cardiovascular

•Class II  
 Secretin like



## REPLACEMENT SHEET



## FIGURE 1C

•Glucagon-like Peptide 1 (GLP-1)	1	Pancreas, Stomach, Lung	Gluconeogenesis	Cardiovascular, Diabetes, Obesity
•Growth hormone-releasing hormone	1	Brain	Neuroendocrine	Growth Regulation
•Parathyroid hormone	1	Bone, Kidney	Calcium Regulation	Osteoporosis
•PACAP	1	Brain, Pancreas, Adrenals	Metabolism	Metabolic Regulation
•Vasoactive intestinal polypeptide (VIP)	1	Gastrointestinal	Motility	Gastrointestinal
•Metabotropic Glutamate	7	Brain	Sensory Perception	Hearing, Vision
•GABA <sub>A</sub>	1	Brain	Neurotransmitter	Mood Disorders
•Extracellular Calcium Sensing	1	Parathyroid, Kidney, GI Tract	Calcium Regulation	Cataracts, GI Tumors
•Class III				



REPLACEMENT SHEET  
**FIGURE 2A**

**G protein-coupled receptors:**

(Division into Class A

Or Class B)

1. **A1 adenosine receptor** [Homo sapiens]. ACCESSION AAB25533  
npivyaf riqkfrvtfl kiwndhfrcq pappidedlp eerpdd  
Class A
2. **adrenergic, alpha -1B-, receptor** [Homo sapiens]. ACCESSION NP\_000670  
npiiypc sskefkrafv rilgcqcrgr grrrrrrrr lggcaytyrp wtrggslers qsrkdsldds gscslgsqrt  
lpsaspspgy lgrgappve lcafepwkap gallspape ppgrgrhds gplftklit epespqtdgg asnggceaaa  
dvangpggfk snmplapgqf  
Class A
3. **adrenergic receptor alpha-2A** [Homo sapiens]. ACCESSION AAG00447  
npviytifn hdfirafkki lcrgrkriv  
Class A
4. **alpha-2B-adrenergic receptor - human**. ACCESSION A37223  
npviytifn qdfiraftri lcrpwtqaw  
Class A
5. **alpha-2C-adrenergic receptor - human**. ACCESSION A31237  
npviyvtfn qdfirpskhi lfrmrgr q  
Class A
6. **beta-1-adrenergic receptor** [Homo sapiens]. ACCESSION NP\_000675  
npiiyers pdfirafqgl lccarraar rhathgdrpr asgclarpgp ppsgaasdd ddddvvgatp parllepwag  
cnggaaadsd ssldepcrpg faseskv  
Class A
7. **beta-2 adrenergic receptor**. ACCESSION P07550  
npiiyersp dfirafqell clrrsslkay gngyssngnt 361 geqsgyhveq ekenklced lpgtedfvgh qgtvpsdnid  
sqgrncstnd sll  
Class A
8. **dopamine receptor D1** [Homo sapiens]. ACCESSION NP\_000785  
npii yafnadfrka fstllgcyl cpatnnaiet vsinnngaam fsshheprgs iskecnlvyl iphavgsedd  
lkkeeaagia rpleklspal svildytdv slekiqpitq ngqhpt  
Class A
9. **D(2) dopamine receptor**. ACCESSION P14416  
npiiyttfn iefirafkli lhc  
Class A



REPLACEMENT SHEET

**FIGURE 2B**

10. **d3 dopamine receptor - human. ACCESSION G01977**  
np viyttfnief rkafikilsc  
Class A
11. **dopamine receptor D4 - human. ACCESSION DYHUD4**  
npviyfv fnaefmvfr kalracc  
Class A
12. **dopamine receptor D5 - human. ACCESSION DYHUD5**  
npviya fnadfqqvfa qlgcsfhcs rtpvetvnis nelisynqdi vfheiaaay ihmmpnavtp gnrevdndec  
egpfdmrfqi yqtspdgdpv aesvweldec geislkitp ftpngfh  
Class A
13. **muscarinic acetylcholine receptor M1 [Homo sapiens]. ACCESSION NP\_000729**  
nmpcyal cnkafdrtdfr lllcrwdkr rwrkiplkpg svhrtpsraq  
Class A
14. **muscarinic acetylcholine receptor M2 [Homo sapiens]. ACCESSION NP\_000730**  
npacy alcnatfkkt fkhllmchyk nigatr  
Class A
15. **muscarinic acetylcholine receptor M3 [Homo sapiens]. ACCESSION NP\_000731**  
n pvcyalcnkt frttfkmlll cqcdkkrk qyqqqsvi fhkrapeqal  
Class A
16. **muscarinic acetylcholine receptor M4 [Homo sapiens]. ACCESSION NP\_000732**  
npa cyalcnatfk ktrfhlllcq yrnigtar  
Class A
17. **m5 muscarinic receptor. locus HUMACHRM ACCESSION AAA51569**  
npicyalcnr tfrktfkml lcrwkkkkve eklywqgnsk lp  
Class A
18. **5-hydroxytryptamine (serotonin) receptor 1A [Homo sapiens]. ACCESSION BAA90449**  
npviy ayfnkdfqna fkiikckf  
Class A
19. **5-hydroxytryptamine (serotonin) receptor 1B [Homo sapiens]. ACCESSION BAA94455**  
npiiyt msnedfkqaf hklirfkets  
Class A
20. **5-hydroxytryptamine (serotonin) receptor 1E [Homo sapiens]. ACCESSION BAA94458**  
n pllytsfnd fklafkkir cre  
Class A

REPLACEMENT SHEET  
**FIGURE 2C**



21. **OLFACTORY RECEPTOR 6A1. ACCESSION O95222**  
npiiyclrnq evkralccil hlyqhqpdp kkgsmv  
**Class A**
22. **OLFACTORY RECEPTOR 2C1. ACCESSION O95371**  
npliy tlmmevkga lrrllgkgre vg  
**Class A**
23. **angiotensin receptor 1 [Homo sapiens]. ACCESSION NP\_033611**  
npl fyglgkfk ryflqllkyi ppkakshsnl sfkmsflsy psdnvssstk kpapcfeve  
**Class B**
24. **angiotensin receptor 2 [Homo sapiens]. ACCESSION NP\_000677**  
npflycf vgnrfqqklr svfrvpitwl qgkresmscr kssslremet fvs  
**Class B**
25. **interleukin 8 receptor beta (CXCR2) [Homo sapiens]. ACCESSION NM\_001557**  
NPLYAFIGQKFRHGLLKILAIHGLISKDSLKPDSRPSFVGSSSGHTSTTL  
**Class B**
26. **cx3c chemokine receptor 1 (cx3cr1) (fractalkine receptor)**  
ACCESSION P49238  
np liyafagekf rrylyhlygk clavlgrsv hvdffssesq rsrhgsvlss nftyhtsdgd allll  
**Class B**
27. **neurotensin receptor - human. ACCESSION S29506**  
n pilynlvsan frhiflatla clcpvwrrr krpafsrkad svssnhflss natretly  
**Class B**
28. **SUBSTANCE-P RECEPTOR (SPR) (NK-1 RECEPTOR) (NK-1R). ACCESSION P25103**  
npiiyccldn rfrlgfkhafrccpfsisagd yeglemkstr ylqtqgsvyk vsrletfistfvgaheepe dgpkatpssl  
dltsncssrs dsktmtesfs fssnvl  
**Class B**
29. **vasopressin receptor type 2 [Homo sapiens]. ACCESSION AAD16444**  
npwiyasfss svsselsll ccargtrpps lgpqdescff asslakdts s  
**Class B**
30. **thyrotropin-releasing hormone receptor - human. ACCESSION JN0708**  
npviy nlmsqkfraa frklcnckqk ptekpanysv alnysvikes dhfstelddi tvtdtlysat kvsfddtcla sevsfsqs  
**Class B**
31. **oxytocin receptor - human. ACCESSION A55493**  
npwiym lftghlfhel vqrfccsas ylkgrlget saskksnsss fvlsrsss q rscsqpsta  
**Class B**

REPLACEMENT SHEET

FIGURE 2D



32. **neuromedin U receptor [Homo sapiens].** ACCESSION AAG24793  
npvlyslmssrfretfqealcigacchrlprhsshslsrmttgstlcdvsgslgswvhplagndgpeaqgetdps  
**Class B**
33. **gastrin receptor.** ACCESSION AAC37528  
nplvy cfmhrrfrqa cletcarcep rpprarpral pdedpppsi aslsrlytt isflgpg  
**Class B**
34. **galanin receptor 3 [Homo sapiens].** ACCESSION 10879541  
nplv yalasrhfra rfrlwpcgr rrrhraral rrvrpassgp pgcpgdarps grllagggqg pepregpvhg geaargpe  
**Class A**
35. **edg-1 - human.** ACCESSION A35300  
npiiy tltnkemrra firimsckc psdgsagkfk rpiiagmefs rkskdnsshp 361 qkdegdnpet imssgnvnss s  
**Class A**
36. **central cannabinoid receptor [Homo sapiens].** ACCESSION NP\_057167  
npiiyalr skdlrhafis mfpscegtaq pldnsmgdsd clkhannaa svhraesci kstvkiavt msvstdtsae al  
**Class A**
37. **delta opioid receptor - human.** ACCESSION I38532  
npvlyaf ldenfkrcfr qlcrkpcgr dpssfsrpre atarervtac tpsdpggggr aa  
**Class A**
38. **proteinase activated receptor 2 (PAR-2) human.** ACCESSION P55085  
dpfvyyfvshdfrdhaknallersvrtvkqmqvsltskkhsrksssyssssttvktsy  
**Class A**
39. **vasopressive intestinal peptide receptor (VIPR) rat.** ACCESSION NM\_012685  
NGEVQAE LRK WRR WHL QGV LGW SSK SQHPW GGS NGATCSTQV SMLTRVSPSARR  
SSSFQAEVSLV  
**Class B**



REPLACEMENT SHEET



**FIGURE 3A**

**Human V2R DNA (nucleotides encoding the last 29 amino acids of the V2R and the adjacent stop codon):**

**gcccggggacgcacccccaccagcctgggtccccaagatgagtcctgcaccaccgccagtcct  
ccctggccaaggacattcatcgtga**

**FIGURE 3B**

**PCR amplified human V2R DNA fragment:**

**gcggccgcacggggacgcacccccaccagcctgggtccccaagatgagtcctgcaccaccgcc  
agtcctccctggccaaggacattcatcgtgaagatctccgcggtctaga**

\*Additions and changes to the V2R DNA are underlined.

\*The Sma I (cccgga) restriction enzyme site (underlined in Fig. 3A) was eliminated in the amplified DNA fragment by changing a cytosine to an adenine.

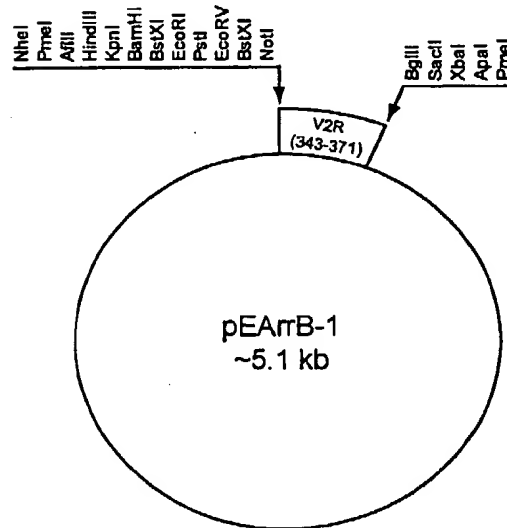
\*A Not I restriction site (gcggccgc) was incorporated into the amplified DNA fragment by adding 6 nucleotides (gcggcc) to the 5' end of the V2R DNA.

\*Bgl II (agatct), Sac II (ccgcgg), and Xba I (tctaga) restriction enzyme sites were added to the 3' end of the V2R DNA.

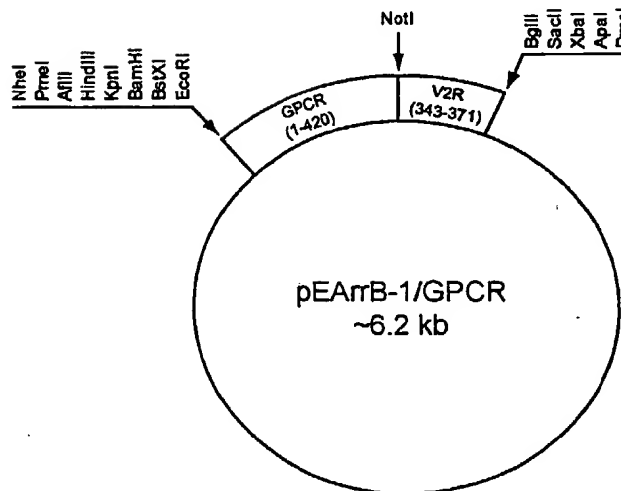
REPLACEMENT SHEET



**FIGURE 4A**



**FIGURE 4B**



**FIGURE 4C**

...AAARGRTPPSLGPQDESCTTASSSLAKDTSS

REPLACEMENT SHEET



FIGURE 7B

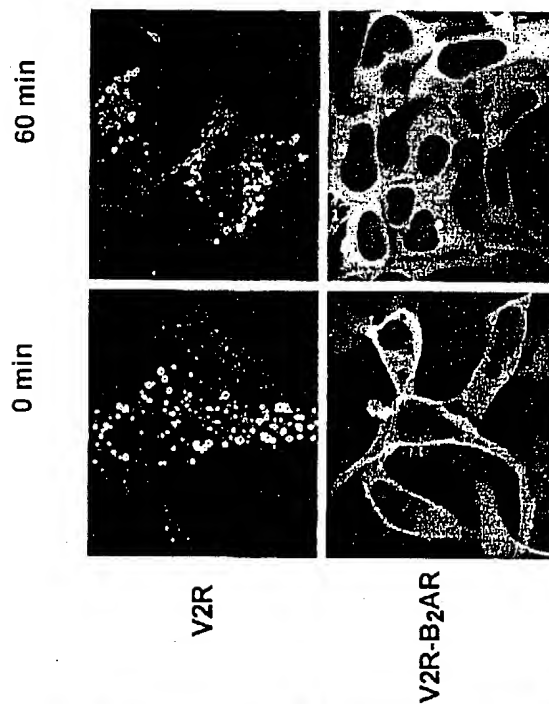
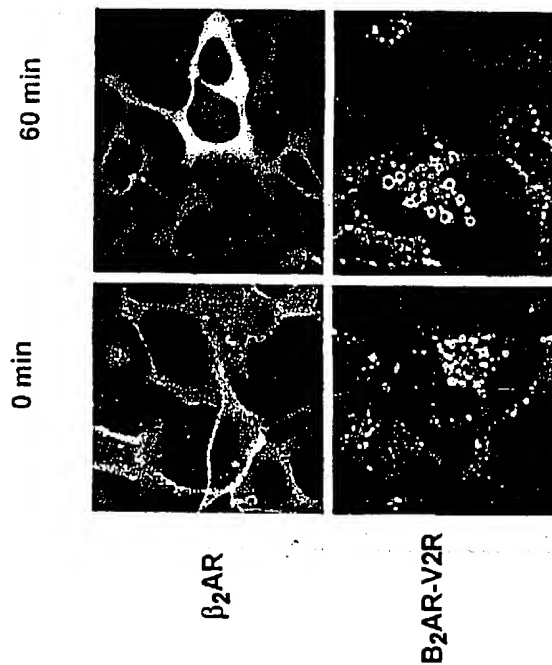


FIGURE 7A



REPLACEMENT SHEET



FIGURE 8A

1) V2R	CARGRTPPSLGPPQDESCTTASSSLAKDTSS
2) V2R-S362X	CARGRTPPSLGPPQDESCTTA
3) V2R-SSSTSS/AAAAAA	CARGRTPPSLGPPQDESCTTAAAAALAKDAAA
4) V2R-TSS/AAA	CARGRTPPSLGPPQDESCTTASSSLAKDAAA
5) V24-SSS/AAA	CARGRTPPSLGPPQDESCTTAAAAALAKDTSS
6) $\beta_2$ AR-V2R-SSS/AAA	CARGRTPPSLGPPQDESCTTAAAAALAKDTSS
7) $\beta_2$ AR	CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP- GTEDFVGHQGTVPDNDISQGRNCSTNDSLL
8) $\beta_2$ AR413-V2R10	CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP- GTEDFVGHQGTVPDNDISQGRNCSTNDSLLSSSLAKDTSS
9) $\beta_2$ AR360-V2R10	CLRRSSLKAYGNGYSSNGNTSSSLAKDTSS

FIGURE 8B

V2R	NPWIYASFSSSVSSELRSLLCCARGRTPPSLGPPQDESCTTASSSLAKDTSS
AAA-1	-----AAA-----
AAA-2	-----AAA-----
NTR-1	NPILYNLVSANFRQVFLSTLACLCPGWRHRRKKRPTFSRKPNSSMSSNHAFSTSATRETLY
AMAA	-----A-AA-----
AAA	-----AAA-----
OTR	NPWIYMLFTGHLFHELVQRFLLCCSASYLKGRRLGETSASKKSNSSSFVLSHRSSQRCSCQPSTA
AAAA	-----AAAA-----
AAA-1	-----AAA-----
AAA-2	-----AAA-----

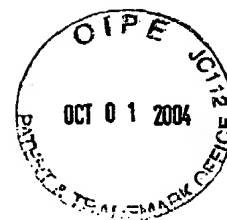
# FIGURE 8C

REPLACEMENT SHEET



SPR	NPIIYCCCLNDRFRLGFKHAFRCPCPFISAGDYEGLMKSTRYLQTOGVYKVSRLTTTISTVGAHEEPEDGPKATPSSLKLTSCSSRSDSKTMTESFSSNVLS
383X	-----X-----
355X	-----X-----
325X	-----X-----
AAIAA	-----AA-AA-----
APAA	-----A-AA-----

REPLACEMENT SHEET



## FIGURE 9A

### Amino Acid Sequence of the Wild-Type Receptors

#### Amino acid sequence of the wild-type V2R

MLMASTTSAPVPGHPSLPSLPSNSSQERPLDTRDPLLARAELALLSIVFVAVALSNGLVLAA  
LARRGRRGHWAPIHVFIGHLCCLADLAVALFQVLPQLAWKATDRFRGPDALCRAVKYLQMGV  
MYASSYMLAMTLDRHRAICRPMLAYRHGSGAHWNRPVLVAVAFSLLLSLPQLFIFAQRNV  
EGGSGVTDWCACFAEPWGRRTYVTWIALMVFVAPTLGIAACQVLIFREIHASLVPGPSERP  
GRRRRGRRTGSPGEGAHVSAAVAKTVRMTLVIVVVVLCWAPFFLVQLWAAWDPEAPLEGA  
PFVLLMLLASLNSCTNPWIYASFSSSVSSELRSLLCCARGRTPPSLGPQDESCTTASSSLA  
KDTSS

(Seq. ID No. 1)

## FIGURE 9B

#### Amino acid sequence of the wild-type $\beta_2$ AR

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMIIVMSLIVLAIVFGNVLVITAIKF  
ERLQTVTNFYFITSACADLMGLAVVPFGAAHILMKMWTFGNFWCEFWTSIDVLCVTASIE  
TLCVIAVDRYFAITSPFKYQSLLTKNKARVILMVWIVSGLTSFLPIQMHWRATHQEAIN  
CYANETCCDFFTQAYAIASSIVSFYVPLVIMVFVYSRVFQEAQRQLQKIDKSEGRFHVQN  
LSQVEQDGRGTGHGLRRSSKFCLKEHKALKTLGIIMGTFTLCWLPPFFIVNIVHVIQDNLIRK  
EVYILLNWIGYVNSGFNPLIYCRSPDFRIAFQELLCLRRSSLKAYGNGYSSNGNTGEQSGY  
HVEQEKENKLLCEDLPGTEDFVGHQGTVPDNDISQGRNCSTNDSLL

(Seq. ID No. 2)

## FIGURE 9C

### Amino Acid Sequence of the Chimeric Receptors

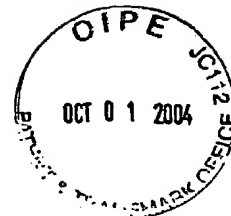
#### Amino acid sequence of the $\beta_2$ AR-V2R chimera (Oakley et al.)

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMIIVMSLIVLAIVFGNVLVITAIKF  
ERLQTVTNFYFITSACADLMGLAVVPFGAAHILMKMWTFGNFWCEFWTSIDVLCVTASIE  
TLCVIAVDRYFAITSPFKYQSLLTKNKARVILMVWIVSGLTSFLPIQMHWRATHQEAIN  
CYANETCCDFFTQAYAIASSIVSFYVPLVIMVFVYSRVFQEAQRQLQKIDKSEGRFHVQN  
LSQVEQDGRGTGHGLRRSSKFCLKEHKALKTLGIIMGTFTLCWLPPFFIVNIVHVIQDNLIRK  
EVYILLNWIGYVNSGFNPLIYCRSPDFRIAFQELL**CARGRTPPSLGPQDESCTTASSSLAK**  
DTSS

(Seq. ID No. 3)

\*shown in bold are the amino acids that were moved to the  $\beta_2$ AR to increase its affinity for arrestin.

REPLACEMENT SHEET



**FIGURE 10A**

**Amino acid sequence of the MOR-V2R chimera expressed from the pEArrB-1/MOR vector**

MDSSTGPGNTSDCSDPLAQASCSPAPGSWLNLSHVDGNQSDPCGLNRTGLG  
GNDSLCPQTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTA  
TNIYIFNLALADALATSTLPPQSVNYLMGTWPFGTILCKIVISIDYYNMFT  
SIFTLCTMSVDRIYAVCHPVKALDFRTPRNAKIVNVCNWILSSAIGLPVMF  
MATTKYRQGSIDCTLTFSHPTWYWENLLKICVFIFAFIMPILIITVCYGLM  
ILRLKSVRMLSGSKEKDRNLRRITRMVLVVAVFIVCWTPIHIVVIAKALI  
TIPETTFQTVSWHFCIALGYTNSCLNPVLYAFDENFKRCFREFCAAARGR  
TPPSLGPQDESCTTASSSLAKDTSS

(Seq. ID No. 4)

**FIGURE 10B**

**Amino acid sequence of the D1AR-V2R chimera expressed from the pEArrB-1/D1AR vector**

MAPNTSTMDEAGLPAERDFSFRILTACFLSLLILSTLLGNTLVCAAVIRFR  
HLRSKVTNFFVISLAVSDLLVAVLVMPWKAVAEIAGFWPFGSFCNIWVAFD  
IMCSTASILNLCVISVDRIYWAISSPFQYERKMTPKAAFILISVAWTLISVLI  
SFIPVQLSWHKAKPTWPLDGNFTSLEDTEDDNCDTRLRSRTYAISSSLISFY  
IPVAIMIVTYTSIYRIAQKQIRRI SALERA AVHAKNCOTTAGNGNPVECAQ  
SESSFKMSFKRETKVLKTL SVIMGVFVCCWLPFFISNCMPFCGSEETQPF  
CIDSITFDVFVWFGWANSSLNPIIYAFNADFQKAFSTLLGCYRLCAAARGR  
TPPSLGPQDESCTTASSSLAKDTSS

(Seq. ID No. 5)

REPLACEMENT SHEET



**FIGURE 10C**

**Amino acid sequence of the 5HT1AR-V2R chimera expressed from the pEArrB-1/5HT1AR vector**

MDVLSPGQGNNNTTSPAPFETGGNTTGISDVTVSYQVITSLLLGTLIIFCAV  
LGNACVVAIALERSLQNVANYLIGSLAVTDLMSVLVLPMAALYQVLNKW  
TLGQVTCDLFIALDVLCTSSILHLCAIALDRYWAITDPIDYVNKRTPRRA  
AALISLTLWLGFLISIPMLGWRTPEDRSDPDACTISKDHGYTIYSTFGAF  
YIPLLLMLVLYGRIFRAARFRIRKTVKKVEKTGADTRHGASAPAPQPKSVN  
GESGSRNWRLGVESKAGGALCANGAVRQGDDGAALVIEVHRVGNSKEHLP  
LPSEAGPTPCAPASFERKNERNAEAKRKMALARERKTVKTLGIIMGTFILC  
WLPFFIVALVLPFCESSCHMPTLLGAI  
INWLGYSNSLLNPVIYAYFNKDFQNAFKKIICKNFCAAARGRTPPSLGPQD  
**ESCTTASSSLAKDTSS**

(Seq. ID No. 6)

**FIGURE 10D**

**Amino acid sequence of the  $\beta$ 3AR-V2R chimera expressed from the pEArrB-1/ $\beta$ 3AR vector**

MAPWPHENSSSLAPWPDLPPTLAPNTANTSGLPGPVWEAALAGALLALAVLAT  
VGGNLLVIVAIAWTPRLQTMNTNFVTSLAAADLVMGLLVPPAATLALTGH  
WPLGATGCELWTSVDVLCVTASIETLCALAVDRYLAVTNPLRYGALVTKRC  
ARTAVVLVWVVSAAVSFAPIMSQWVRVGADAEQRCHSNPRCCAFASNMPY  
VLLSSSVSFYLP LLVMLFVYARVFV VATRQLRLLRGELGRFPPEESPAPS  
RSLAPAPVGTCPPEGVPACGRRPARLLPLREHRALCTLGLIMGTFTLCWL  
PFFLANVLRALGGPSLVPGPAFLALNWLGYSANSAFNPLIYCRSPDFRSAFR  
RLLCRCAAARGRTPPSLGPQDESCTTASSSLAKDTSS

(Seq. ID No. 7)

**FIGURE 10E**

**Amino acid sequence of the Edg1R-V2R chimera expressed from the pEArrB-1/Edg1R vector**

MGPTSVPLVKAHRSSVSDYVNYDIIVRHNYTGKLNISADKENS IKLTSV  
FILICCFIILENIFVLLTIWTKKFHRPMYYFIGNLALS DLLAGVAYTANL  
LLSGATTYKLTPAQWFLREGSMFVALSASFSLAIAIERYITMLKMKLHN  
GSNNFRLFLLISACWVISLILGGLPIMGWNCISALSSCSTVLPLYHKHYIL  
FCTTVFTLLLLSIVILYCRIYSLVRTRSRLTFRKNISKASRSSEKSLALL  
KTVIIVLSVFIACWAPLFILLLLDVGCKVKTC DILFRAEYFLVLAVLNSGT  
NPIIYTLTNKEMRRAFIRIMSCCKCAAARGRTPPSLGPQDESCTTASSSLA  
**KDTSS**

(Seq. ID No. 8)





REPLACEMENT SHEET

**FIGURE 11A**

**Nucleotide sequence of the  $\beta$ 2AR-V2R chimera**

atggggcaaccggaacggcagcgcccttcttgctggcacccaatagaagccatgcgccggacc  
acgacgtcacgcagcaaagggacgaggtgtgggtgggcatgggcatcgatgtctctcat  
cgtcctggccatcgtgtttggcaatgtgctgggtcatcacagccattgccaaagtgcgagcgtctg  
cagacggtcaccaactacttcatcacttcaactggcctgtgctgatctgggtcatgggcctggcag  
tggtgccctttggggccgcccattattcttatgaaaatgtggacttttggcaacttctgggtgcga  
gttttggacttccattgatgtgctgtgctgcacggccagcattgagaccctgtgctgatcgca  
gtggatcgctactttgccattacttcaactttcaagtaccagagcctgctgaccaagaataagg  
ccgggtgatcattctgatgggtgtggattgtgtcaggccttacctccttcttggccattcagat  
gcaactggtacggggccaccaccaggaagccatcaactgctatgccaatgagacctgctgtgac  
ttcttcacgaaccaagcctatgccattgaccttccatcggtgtccttctacgttcccctgggtga  
tcatgggtcttcgtctactccagggtcttccaggaggccaaaaggcagctccagaagattgacaa  
atctgagggcgcttccatgtccagaaccttagccagggtggagcaggatgggcggacggggcat  
ggactccgcagatcttccaagtctctgcttgaggagcacaagccctcaagacgttaggcattca  
tcatgggcaactttcacctctgctggctgcccttcttcatcggttaacattgtgcatgtgatcca  
ggataacctcatcgtaaggaagtttacatcctcctaaattggataggctatgtcaattctgggt  
ttcaatccccttatctactgcccggagcccagatttcaggattgccttccaggagcttctgtgcg  
ccgggggacgcaccccaccagcctgggtccccaagatgagtcctgcaccaccgccagctcctc  
cctggccaaggacacttcatcgtaga

(SEQ ID No. 9)

**FIGURE 11B**

**Nucleotide sequence of the MOR-V2R chimera**

atggacagcagcaccggcccagggaacaccagcgactgctcagaccccttagctcaggcaagtt  
gtccccagcacctggctcctggctcaacttgtcccacggtgatggcaaccagtcgatccatg  
cggctctgaaccgcaccgggcttggcggggaacgacagcctgtgccctcagaccggcagccctcc  
atgggtcacagccattaccatcatggccctctactctatcgtgtgtgtagtgggcctcttcggaa  
acttccctgggtcatgtatgtgattgtgaagatacaccaaaaatgaagactgccaccaacatctacat  
tttcaaccttgctctggcagacgccttagcgaccagtagcactgccccttccagagtgtcaactac  
ctgatgggaacatggcccttcgggaaccatcctctgcaagatcgatgatctcaatagattactaca  
acatgttcaccagcatattcacctctgcaccatgagcgtggaccgctacattgctgtctgcca  
cccagtc aaagccctggatttccgtaccccccgaaatgccaaaatcgtaacgtctgcaactgg  
atcctctcttctgcccacggtctgctgtaatgttcatggcaaccacaaaatacaggcaggggt  
ccatagattgcaccctcacgttctcccacccaacctggtagtgggagaacctgctcaaaatctg  
tgtctttatcttgcctttcatcatgcgatcctcatcatcactgtgtgttacggcctgatgatc  
ttacgactcaagagcgttcgcatgctatcgggctccaagaaaaggacaggaatctgcgcagga  
tccccggatgggtgctgggtgggtcgtggctgtatttatcgtctgctggacccccatccacatcta  
cgtcatcatcaaagcgtgatcacgattccagaaaccacatttcagaccgttctcctggcacttc  
tgcattgctttgggttacacgaacagctgcctgaatccagttctttacgccttctcctggatgaaa  
acttcaagcgtatgcttcagagagttctgcgcggcgccacgggggacgcaccccaccagcctggg  
tccccaagatgagtcctgcaccaccgccagctcctccttggccaaggacacttcatcgtaga

(SEQ ID No. 10)

REPLACEMENT SHEET

FIGURE 11C

Nucleotide sequence of the D1AR-V2R chimera

atggctcctaacttctaccatggatgagggcgggctgccagcggagagggatttctcctttc  
gcacctcacggcctgtttcctgtcactgtcactcctgtccactctcctgggcaatacccttgt  
ctgtgcggcgtcatccggtttcgacacctgaggtccaaggtgaccaacttctttgtcatctct  
ttagctgtgtcagatctcttgggtggctgtcctgggtcatgccctggaaagctgtggccgagattg  
ctggccttttggccctttgggtccttttgtaacatctgggtagcctttgacatcatgtgctctac  
ggcgtccattctgaacctctgctgtatcagcgtggacaggtactgggctatctccagccctttc  
cagtatgagaggaagatgacccccaaagcagccttcactcctgattagcgtagcatggactctgt  
ctgtccttatatccttcacccagtacagctaagctggcacaaggcaaagcccacatggccctt  
ggatggcaattttacctccctggaggacaccgaggatgacaactgtgacacaagggtgagcagg  
acgtatgccatttcacgtccctcatcagcttttacatccccgtagccattatgatcgtcacct  
acaccagtatctacaggattgcccagaagcaaaccggcgcatctcagccttggagagggcagca  
gtccatgccaagaattgccagaccacgcaggtaacgggaaccccgctcgaatgcgccagctctg  
aaagtccctttaagatgtccttcaagagggagacgaaagtcttaagacgctgtctgtgatcat  
gggggtgtttgtgtgctgctggctccctttcttcactctcgaactgtatgggtgcccttctgtggc  
tctgaggagaccagccattctgcatcgattccatcaccttcgatgtgtttgtgtgggttgggt  
ggcggaattcttccctgaacccattatttatgcttttaatgctgacttccagaaggcgttctc  
aacctcttaggatgctacagactctgcgcggcgccagcggggacgcacccaccagcctgggt  
ccccaagatgagtcctgcaccaccgcagctcctccctggccaaggacacttcacgtga  
(SEQ ID No. 11)

FIGURE 11D

Nucleotide sequence of the 5HT1AR-V2R chimera

atggatgtgctcagccctgggtcagggcaacaacaccacatcaccaccgggtccctttgagaccg  
gcggcaacactactggatatctccgacgtgacgtcagctaccaagtgatcacctctctgctgct  
gggcaagctcatcttctgcgcgggtgctgggcaatgcgtgctgggtggctgccatgccttggag  
cgctccctgcagaacgtggccaattatcttattggctctttggcggtcacgacctcatgggtgt  
cggtgttgggtgctgcccattggccgcgtgtatcaggtgctcaacaagtggacactgggcccagg  
aacctgcgaacctgttcacgcctcgcagctgctgtgctgcacctcatccatctgcacctgtgc  
gccatcgcgtggacaggtactgggccatcacggaccccatcgactacgtgaacaagaggacgc  
cccggcgcgcgctgcgtcatctcgtcacttggcttattggcttctcatctctatcccgcc  
catgctgggtggcgacccccggaagaccgctcggacccccgacgcatgcaccattagcaaggat  
catggctacactatctattccaccttggagctttctacatcccgctgctgctcatgctgggttc  
tctatgggcgcataattccgagctgcgcgcttccgcatccgcaagacggtcaaaaagggtggagaa  
gaccggagcggacaccgcctatggagcatctccgccccgcagcccaagaagagtgtgaatgga  
gagtcgggggagcaggaactggaggctgggcgtggagagcaaggctgggggtgctctgtgcgcca  
atggcgcggtgaggcaagggtgacgatggcgccgcctggagggtgatcgagggtgcaccgagtggg  
caactccaaagagcacttgccctctgccagcagaggctggctcctacccttgtgccccgcctct  
ttcgagaggaaaaatgagcgcaacgccgaggcggaagcgcaagatggccctggccccgagagagga  
agacagtgaagacgctgggcatcatcatgggcaccttcacctctgctgggtgcccttcttcat  
cgtggctcttgttctgcccttctgcgagagcagctgccacatgccaccctgttgggcgcata  
atcaattggctgggctactccaactctctgcttaaccccgctcatttacgcatacttcaacaagg  
actttcaaaacgcgtttaagaagatcattaagtgtaaactctgcgcggcgccagcggggacgcac  
cccaccagcctgggtcccccaagatgagtcctgcaccaccgcagctcctccctggccaaggac  
acttcacgtga  
(SEQ ID No. 12)



REPLACEMENT SHEET

FIGURE 11E

Nucleotide sequence of the  $\beta$ 3AR-V2R chimera

atggctccgtggcctcacgagaacagctctcttgcgccatggccggacctccccaccctggcgc  
ccaataccgccaacaccagtgggctgccaggggttcctgtgggaggcgccctagccggggccct  
gctggcgctggcggtgctggccaccgtgggaggcaacctgctggtcatcgtggccatcgccctgg  
actccgagactccagaccatgaccaacgtgttcgtgacttcgctggccgcagccgacctggtga  
tgggactcctggtggtgccgcccggcgccaccttggcgctgactggccactggccgttggggcg  
cactggctgcgagctgtggacctcggtggacgtgctgtgtgtgaccgccagcatcgaaacctg  
tgcgccctggccgtggaccgtacctggctgtgaccaaccgctgcgttaaggcgccactggtca  
ccaagcgtgcgcccggacagctgtggtcctggtgtgggtcgtgtcgcccgcggtgtcgtttgc  
gcccacatcatgagccagtgggtggcgcgtagggggcgacgcccaggcgagcgctgccactccaac  
ccgcgctgctgtgccttcgcctccaacatgcctacgtgctgtcctcctcgtctccttct  
accttcctcttctcgtgatgctcttcgtctacgcgcgggttttcgtgggtggctacgcgccagct  
gcgcttgcgtgcgcggggagctggggccgcttccgcccaggagctcctccgcggcgccgtcgcg  
tctctggccccggccccgggtggggacgtgcgctccgcccgaagggtgcccgcctgcggccggc  
ggccccgcgcgcctcctgcctctccgggaacaccgggcccctgtgcaccttgggtctcatcatggg  
caccttcactctctgctggttgccttcttctggccaacgtgctgcgcgcctggggggcccc  
tctctagtcccgggccccgggttctcttgccctgaactggctagggtatgccaatctgccttca  
accgctcatctactgcgcagcccggaacttcgcagcgccctccgccgtcttctgtgcgcgtg  
cgcgccgcgaacggggacgcacccccaccagcctgggtccccaagatgagtcctgcaccaccgcca  
gtcctccttggccaaggacacttcatcgtga

(SEQ ID No. 13)

FIGURE 11F

Nucleotide sequence of the Edg1-V2R chimera

atggggcccaccagcgtcccgctggtcaaggcccaccgcagctcggtctctgactacgtcaact  
atgatcatcatcgtccggcattacaactacacgggaaagctgaatatcagcgccggaaggagaa  
cagcattaaactgacctcggtggtgttcattctcatctgctgctttatcatcctggagaacatc  
tttgtcttgetgaccatttggaaaaccaagaaattccaccgacctatgtactattttattggca  
atctggccctctcagacctgttggcaggagtagcctacacagctaacctgctcttgtctggggc  
caccacctacaagctcactcccgcccagtggtttctgcgggaaggagtagtattgttggccctg  
tcagcctccgtgttcagtctcctcgccatcgccattgagcgctatatcacaatgctgaaaatga  
aactccacaacgggagcaataacttcgcctcttctgctaatcagcgccctgctgggtcatctc  
cctcatcctgggtggcctgcctatcatgggctggaactgcatcagtgcgctgtccagctgctcc  
accgtgctgcgcgtctaccacaagcactatctcctcttgcaccacggctcttcactctgcttc  
tgctctccatcgtcattctgtactgcagaatctactccttgggtcaggactcggagccgcgcct  
gacgttccgcaagaacatttccaaggccagccgcagctctgagaagtcgctggcgctgctcaag  
accgtaattatcgtcctgagcgtcttcatcgccctgctgggcaccgctcttcatcctgctcctgc  
tggatgtgggctgcaagggtgaagacctgtgacatcctcttcagagcggagtagtctcctgggtgt  
agctgtgctcaactccggcaccacccccatcatttacactctgaccaacaaggagatgcgtcg  
gccttcatccggatcatgtcctgctgcaagtgcgcggccgcacggggacgcacccccaccagcc  
tgggtccccaagatgagtcctgcaccaccgcccagctcctccttggccaaggacacttcatcgtg

a

(SEQ ID No. 14)

